

# Literature Search for Alternatives Worksheet

This worksheet is designed to assist researchers, information specialists, and IACUC members who are conducting literature searches to determine if alternatives exist and to determine whether the protocol unnecessarily duplicates previous research. When searching for alternatives, the Animal Welfare Information Center (AWIC) refers to the 3R's of W.M.S. Russell and R.L. Burch described in their book *The Principles of Humane Experimental Technique* (1959). The 3R's are: reduction in the number of animals used, refinement of techniques and procedures to reduce pain or distress, and replacement of animals with non-animal techniques or use of less-sentient species. The worksheet uses AWIC's two-phase approach to searching for alternatives, which addresses both unnecessary duplication and the 3R's of alternatives (see *worksheet instructions for more details*). The worksheet requests information needed to retrieve keywords and concepts from the protocol, develop a search strategy, and run a multi-database literature search for alternatives.

1. **Principal Investigator:** \_\_\_\_\_  
**Phone number:** \_\_\_\_\_  
**Email address:** \_\_\_\_\_
2. **Title of Animal Study Protocol:**
3. **General area of study:** (e.g., drug testing, cardiology, toxicology, fetal alcohol syndrome, lipid metabolism, etc.)
4. **Type of protocol:** Is the proposed study a research, teaching, or testing protocol?
5. **Proposed animal species:** (e.g., swine, rats, dogs, primates, etc.)
6. **Describe your experimental protocol including objectives and endpoints:**
7. **Identify the biological systems or anatomy involved in the study** (e.g., lung, central nervous system, kidney, etc.)
8. **List any drugs or compounds used in procedures.** (e.g., anesthetics, analgesics, test compounds, etc.)
9. **Describe the methods and procedures using animals and the relevance to the study, paying particular attention to those procedures that may cause pain or distress to the animal.**
10. **List any potential alternatives (3Rs of Reduction, Refinement and Replacement) of which you are aware.** (e.g., alternate models, modified techniques, housing modifications, modified restraint, in vitro methods, computer simulations, etc.)
11. **List key keywords/concepts using terminology from your responses to questions above. Keeping your concepts separate will assist you in creating a good search strategy.**  
(e.g. Keywords of concept 1 - *heart or cardiac or cardiovascular disease* (include synonymous terms)  
and  
Keywords of concept 2 - *atherosclerosis or arterial plaques* (include synonymous terms))

**12. Database selection:** (Choose those that are appropriate for the area of study):

\_\_\_\_ MEDLINE (PubMed) \_\_\_\_ EMBASE \_\_\_\_ BIOSIS \_\_\_\_ CAB

\_\_\_\_ AGRICOLA \_\_\_\_ TOXNET \_\_\_\_ NTIS \_\_\_\_ FEDRIP \_\_\_\_ Current Contents

\_\_\_\_ Other specialized databases and web resources (i.e., Zoological Record, Lifesciences, PsycINFO, ERIC, ASFA, DTIC, PrimateLit, InvitroDerm, AVAR's Alternatives in Education Database, NORINA's Audiovisual Database, Altweb's Anesthesia/Analgesia and Humane Endpoints Databases, AnimAlt-ZEBET Database, etc.)

**13. Publication year(s) covered:** \_\_\_\_\_ to \_\_\_\_\_

**14. List any other methods used to determine that alternatives are/are not available:** This should be secondary to the literature search, and it may be useful to support or rebuke potential alternatives found in the search. Examples of other sources are: conference attendance, committee membership, professional expertise, training, etc.

For additional information on completing this form contact your IACUC, information specialist, or the AWIC web site at [www.nal.usda.gov/awic/alternatives/alternat.htm](http://www.nal.usda.gov/awic/alternatives/alternat.htm), where you can find sample searches, methods and guidelines, training and education, databases, organizations, and other resources that can assist in understanding alternatives, finding alternatives and completing the alternatives search.

**Other resources:**

**Consideration of Alternatives to Painful/Distressful Procedures – USDA/APHIS/AC - Policy #12**  
<http://www.aphis.usda.gov/ac/policy/policy12.pdf>

***The Principles of Humane Experimental Technique* by Russell and Burch**  
[http://altweb.jhsph.edu/publications/humane\\_exp/het-toc.htm](http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm)

**AWIC Tips for Searching for Alternatives to Animal Research and Testing**  
<http://www.nal.usda.gov/awic/alternatives/tips.htm>

**Department of Defense Animal Care and Use Program Appendices**  
<http://www.dtic.mil/biosys/downloads/Appendicies.PDF>

Created by

D'Anna Jensen and Michael Kreger  
USDA, NAL, Animal Welfare Information Center (AWIC)  
10301 Baltimore Ave. – 4<sup>th</sup> floor  
Beltsville, MD 20705  
Phone: 301-504-6212  
Fax: 301-504-7125  
Email: [awic@nal.usda.gov](mailto:awic@nal.usda.gov)  
Website: [www.nal.usda.gov/awic](http://www.nal.usda.gov/awic)

# Worksheet Instructions for the Literature Search for Alternatives

The worksheet is a tool used to 1) familiarize the information specialist, principal investigator, attending veterinarian or IACUC with the protocol; 2) identify keywords and concepts that are important in the development of a search strategy; 3) aid in the selection of appropriate topical databases or other on-line resources. Although this worksheet will help, it is not designed as a replacement for open communication between information providers, investigators, veterinarians, and IACUC members. In order to conduct a proper alternatives search, direct dialogue is recommended between the researcher and the person conducting the search. A third person should not be used to convey information.

Once the worksheet has been filled out, the person conducting the search can proceed with creating a search strategy for alternatives by dividing it into two phases: 1) reduction and refinement (unnecessary duplication is addressed here) and 2) replacement.

During Phase 1 of the search, the reduction and refinement aspects of the study are emphasized. The use of analgesics and analgesia, the use of remote telemetry to increase the quality and quantity of data gathered, and humane endpoints for the animals are examples of refinements. Use of shared control groups, preliminary screening in non-animal systems, innovative statistical packages or a consultation with a statistician are examples of reduction alternatives.

In order to create a search strategy to address Phase 1, keywords and concepts from the area of research are used. Because reduction and refinement aspects of alternatives are broad and often are addressed in the methods section of studies, the search at this point is really a comprehensive look at the field of study. This in turn addresses whether the protocol unnecessarily duplicates prior research. Upon completion of Phase 1, there should be a basic understanding of the research area including: 1) the literature published in the particular field, 2) the techniques used, and 3) the commonly used species.

Now you are ready to address Phase 2 – replacement. This is where you want to address potential alternatives such as cell culture, tissue culture, models, simulations, etc. This is also where you might look for any alternate animal models lower on the phylogenetic scale—fish or invertebrates, for example—that would still give you the data you need.

It is important to become familiar with the database systems or other resources available at your institution in order to properly execute the alternatives search. The institution's librarian or information specialist can help with this and should be consulted. For example, some database systems allow truncation of keywords using a ? (i.e., "rodent?" gives "rodent" or "rodents"), while other systems use the symbol \*.

Additional instructions for each point on the worksheet:

1. **Contact Information.** This is very useful if those conducting the search have questions.
2. **Protocol Title.** The title of the protocol may provide some keywords.
3. **General area of study.** Keep this broad. These keywords can be used to limit the search to the desired subject area. Examples are cardiac, anesthesia, AIDS, transgenics, etc.

4. **Type of protocol.** Search strategies for research, teaching, or testing protocols differ. For example, a teaching protocol might include keywords such as "teach," "educate," or "instruct," while a testing protocol could include "safety," "efficacy," or "test".
5. **Proposed animal species.** The animal model may be used as a keyword in the reduction and refinement phase of the search. At times the animal species is not initially used in the search in order to determine if the study can be done in alternate models. Is there a unique quality or usefulness about your chosen species that warrants its selection? Providing this may provide additional keywords or eliminate the need to search for other possible models being used.
6. **Protocol description.** Provide a complete description of the proposed use of animals. This section should succinctly outline the scientific plan and direction of the experiment. When doing a keyword search on multiple databases simultaneously, the database system searches for words that appear in the title, abstract, and descriptor fields of the citation. Because the painful part of the procedure may be described in the materials and methods sections, the search should focus on the experimental endpoint or objective in most cases. Exceptions are when methodology papers are common in the field of study (i.e., skin irritation tests, antibody production). Humane endpoints, such as indicators of pain, or euthanasia, can be useful in searches to determine when the animal should be removed from the study. While endpoints are not easily searchable, they are worth considering when reviewing the search results.
7. **Systems or anatomy.** Providing specific systems, parts of the anatomy, or structures may assist in limiting the search (i.e. cerebellum, arterial, nephrons, etc.).
8. **Drugs or compounds.** Give specific names of drugs you may be using for your study or as anesthetics or analgesics. (i.e. halothane, rompun, buprenorphine, etc.). Remember to include the scientific and generic name of the drugs. If you are using other compounds in your study, please list them. This is helpful when you search the literature for drugs that may conflict or have contraindications with your area of study. Much of this sort information may not be common knowledge.
9. **Methods and procedures.** Providing the methods and procedures used in your animal study protocol will assist in addressing issues of refinement alternatives, such as handling techniques, restraint techniques, injection techniques, surgical procedures, etc. Identification of any painful procedure is appropriate at this point, along with drugs or methods that will be used to relieve the pain. The law defines a painful procedure as one that would "reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied." If a procedure involves pain or distress, the PI must consult with the attending veterinarian.
10. **Potential alternatives.** Listing terms to describe any *potential* alternatives you are aware of, such as in vitro, tissue culture, alternative procedures or alternative animal models, etc. is helpful in conducting the refinement alternative aspect of the search. It is also helpful in determining potential terms to use, since these are terms outside the specific area of study.
11. **Keywords, concepts and ultimate search strategy.** These are words that will likely be found in the title, abstract, and descriptor fields of the citation. Use as many synonyms as possible, such as "cardiac" and "heart." Include acronyms and complete spellings (i.e., "GH" and "growth hormone"). Also include all possible spellings of words. For example, "anesthesia," "anesthetic," and "anaesthesia." Include words that make the study different from other studies. This will help detect unintentional duplication as well as limit the scope of the search if the number of citations from a broader search is more than 200. All potential alternatives should be included as keywords, whether or not the researcher believes they will be useful. They will be used in the replacement phase of the search.

The search strategy consists of the reduction and refinement phase and the replacement phase as mentioned above. Using the keywords selected from parts 3 through 8 on the worksheet, put together brief strings of words so that each search set covers a separate concept. For example, the first set might include words relating to the experimental outcome, and the second set will contain words relating to the animal model. Short and simple search sentences can later be combined. The reduction and refinement phase should be similar to the typical literature review done in preparation for a new project or scientific publication. Keywords used will help the researcher determine if there is unintentional duplication, how many animals are necessary using the proposed model, appropriate anesthetics and analgesics, and any other method of minimizing pain and distress. Since much of the refinement and reduction information will be found in the materials and methods sections, it is important for the researcher to review some of the articles that may be of interest.

Many people make the mistake of putting the term "alternatives" in the strategy and expect to find all possible alternatives. Because alternatives is a complex concept involving refinement, reduction and replacement, this term is best used only in those areas of study where larger amounts of research have been conducted on alternatives, such as in toxicology or education. They might also end up with "alternatives" that have nothing to do with the 3Rs.

The replacement phase should include keywords for potential alternatives such as "vitro," "culture," or simulation." The word "alternative" may also be included here. The selected animal model, other species, and the word "model" will help retrieve animal and non-animal models as potential alternatives.

***NOTE: It is very important to realize that stringing together keywords on one line (i.e., dogs or cats and cardiac or thoracic and stent or device and alternative) does not create a proper search strategy and results in a poor search with inaccurate results.***

- 12. Database selection.** The worksheet lists some of the most popular databases for biomedical research topics. Although there is some overlap in journals and other publications covered by the databases, each database is unique. A search of MEDLINE should also include EMBASE since EMBASE includes monographs, reports, and European research not included in MEDLINE. Several of the core databases should be searched in order to conduct a comprehensive literature search. Keep in mind the type of protocol when choosing databases. An education protocol, for example, should include ERIC; a protocol involving testing toxic effects of compounds should include TOXNET and RTECS. There are many other specific databases available on-line – both free and subscription based.
- 13. Years of coverage.** When a database is chosen on CD-ROM, the World Wide Web, or on a multi-database system, the publication years covered are listed near the title of the database. The searcher should record the years included in the search based on database coverage or the years selected by the searcher within the search strategy (i.e., 1988-2003).
- 14. Other methods.** The Animal Welfare Act regulations and policies allow for researchers to describe other methods and sources used to determine the availability of alternatives. While this should be secondary to the literature search, it should be mentioned, particularly to support or rebuke potential alternatives found in the search. Other methods and sources include conference attendance, committee membership, professional expertise, and training.